IV REUNIAO CONJUNTA DAS SOCIEDADES PORTUGUESA E ESPANHOLA DE FARMACOLOGIA

Fevereiro 28, Março 1 e 2, 1991

LISBOA, PORTUGAL

FACULDADE DE CIÊNCIAS MÉDICAS
DEPARTAMENTO DE FARMACOLOGIA

Title: INACTIVATION OF THE CORTICOID CICLESONIDE BY HEPATIC OXYDASES

Author: Mª P. MARTINEZ; J.M. MASSO; J.R. CONDE; R. DE LA FUENTE
I+D Division - Laboratorios ELMU, S.A. (Madrid)

The objective of this work is to assess the influence of the hepatic oxydases on the metabolism of the corticoids Ciclesonide and Budesonide by measuring the systemic activity, administering these substance p.o. or s.c. in three dose levels, to rats who have or have not been treated previously with SKF 525-A* (50 mg/kg i.p.).

This compound is a potent inhibitor of the hepatic oxydases.

Ciclesonide s.c., does not show significative differences between the results obtained with and without SKF 525-A: 66.7 and 64.1% thymus inhibition respectively in the highest dose. At the same dose p.o. it shows and inhibition of 6.2% without SKF 525-A and 45.9% with SKF 525-A ($p<0.05$).

Budesonide s.c. does not show significative differences between its action with and without SKF 525-A, in both cases, the systemic action is high (approximately 80% thymus inhibition, in the highest dose).

The oral administration of Budesonide shows significative differences at all doses on the thymus with and without SKF 525-A. All inhibitions are situated between 60 and 70% in the first case and between 20 and 30% in the second one.

Under normal metabolic conditions, it is observed that the systemic activity of the compounds administered p.o. is lower than the systemic action s.c., which is indicative of existence of a hepatic metabolic process in the initial step which is very effective in both corticoids. Therefore it is confirmed that the systemic action of ciclesonide is lower than the action of budesonide by both routes of administration.

The results of this experience indicate that ciclesonide presents a moderated oral absorption and an almost total subsequent hepatic metabolism.

In contrast, budesonide presents a high degree of gastrointestinal absorption, although suffering an hepatic metabolism which inactives a great extent of its systemic activity.

(*) SKF 525-A was a gift from Lab. SK & F.